UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/339,352	06/23/99	REED-GITOMER	B	UTSD:553

HM22/1107

MARK B WILSON
ARNOLD WHITE & DURKEE
PO BOX 4433
HOUSTON TX 77210-4433

EXAMINER	
ROBINSON, H	
ART UNIT	**PAPER NUMBER**
1653	10

DATE MAILED: 11/07/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/339,352	Reed-Gitomer et al.
Examiner	**Group Art Unit**
Hope Robinson	1653

☒ Responsive to communication(s) filed on *Aug 17, 1900*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-7, 10-15, and 17* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7, 10-15, and 17* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's response to the Office Action mailed April 12, 2000 in Paper No. 10 on August 17, 2000 is acknowledged.

2. Applicant's cancellation of Claim 8 is acknowledged. Claims 10-12 have been amended. Claims 1-7, 10-15 and 17 are pending.

3. The following grounds of rejection are or remain applicable:

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 (e) as follows:

The second application (which is called a continuing application) must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the continuing application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *In re Ahlbrecht*, 168 USPQ 293 (CCPA 1971).

The examiner read the provisional application and did not find support for sequences recited in the claims and disclosed in the specification (SEQ ID No. 1 which encodes the protein contained in SEQ ID No.2) of the current application. Furthermore, the provisional application did not disclose the marker D1S2681 wherein the genomic region of the invention is comprised. Therefore, this application will not get the Priority date of the provisional application in regard to the present claims but only the filing date of the present application which is June 23, 1999.

Applicant's arguments filed on August 17, 2000 in Paper No. 9 asserts that while additional material provided when the provisional application was converted to the instant application, it is nevertheless improper to assert that the full scope of the claims as currently pending were not taught by the original provisional application. Further that the claim scope is enabled by the initial provisional application . As stated above the provisional application does not provide adequate support see for example claims 10 and 12 where the marker D1S2681 wherein the genomic region of the invention is comprised is not disclosed and none of the sequences contained in the present application. Thus, the with holding of the priority date is maintained because the application remains non-compliant with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 (e).

Claim Rejections-Utility Rejections Under 35 USC § 101 And 35 USC 112, First Paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-7, 10-15 and 17 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility based on screening for increased risk of developing hypercalciuria by testing for mutation(s) at/in chromosome 1q23.3-1q24. The present application on page 5, refers to the invention as "relating to the discovery that there exists an area on human chromosome 1 that is genetically linked to absorptive hypercalciuria (AH), and thus to some forms of osteoporosis as well. However, no discussion is provided as to where the mutation demonstrates an increased risk for AH or what mutation was to have been detected. The disclosure simply states that the present invention involves a simple, straightforward genetic test that can be implemented in diagnosing SH and osteoporosis with hypercalciuria (see page 6) which indicates the gene involved in Ah would need to be identified by refining the locus. Additionally, the disclosure also states that the genomic region associated with an increased risk of AH may have a sequence contained in at least one genetic sequence selected from the grouping provided in Claim 12.

The specification does not clearly set forth how a standardized screening method would be developed to screen for increased risk of AH. Applicant discloses that the genomic region associated with an increased risk of AH may localize to more than one gene in this area, and that it is expected that there are several unique mutations associated with an increased risk of AH in different individuals (see page 123). This much variability goes against the specification assertion that the invention provides a simple genetic test for increased risk of AH (see page 6). Furthermore, the specification on page 123 asserts that AH is inherited in an autosomal dominant mode due to a gene mutation in the chromosome 1q23.3-1q24 locus and that based on the map of chromosome 1 no genes of known function have been identified in this candidate region. Moreover, page 7 of the present specification indicates the genetic material of SEQ ID No. 1 is only putative and is not yet characterized whereas page 118 lines 5-10 of the application indicate an inherited defect is one likely cause of AH. The examples (1-7) do not demonstrate nor describe the claimed "...screening for increased risk...". In view of the foregoing, and absent data/evidence, the claimed invention lack utility. Since the specification sets forth no specific mutation, the claimed screening/detecting method lack a specific and substantial utility.

The assertion that a gene mutation in the chromosome 1q23.3-1q24 is responsible for AH on page 123 of the specification and the claim made of a simple genetic test to screen for increased risk of AH followed by a discussion of the uncertainty of the gene region genes and variability of the mutation, may be indicia of a "real world" use, but in view of the absence of

disclosure in the application of working examples (i.e. data) and complete details for carrying out the processes indicated in the claims, the utility indicated would require further experimentation.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-8, 10-15 and 17 remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-7, 10-15 and 17 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite and the dependent claims hereto because species (a) does not define what mutation is being detected. Furthermore, the claim is indefinite because it is unclear how species (b) relates to an increased risk. The claim is also indefinite because of the amendatory language "wherein said genomic region is comprised in chromosome 1q23.3-1q24". It is also not demonstrated where nor clear how the mutation causes increased risk.

Applicant's arguments filed on August 17, 2000 in Paper No. 9 asserts that "in order to satisfy the requirements of definiteness..., a claim, read in light of the specification...". Applicant is correct, however, the limitations of the specification cannot be read into the claims. Claim 1 is indefinite because the claim broadly recites "to detect the presence or absence of a genetic mutation" and does not provide any indicia of how species (b) relates to an increased risk of developing hypercalciuria because the method step does not set forth clearly how this will be achieved. In addition, the response asserts that "while the mutation is obviously the basis of the detected chromosomal alteration, elucidation of the specific nucleotide change is not at this point necessarily pertinent to the ability to successfully screen for the change". However, the claimed method is directed to detecting the presence or absence of a genetic mutation. Therefore, if the specific nucleotide change is not indicated then it is unclear how the method will function. Further, does any genetic mutation result in increased risk for hypercalciuria? Additionally, applicant asserts that it is unclear what the Office action deems objectionable about the amendatory language or why the failure to demonstrate where the mutation causes increased risk is an issue in the determination of definiteness. The claim is indefinite because it is unclear how

finding a mutation is equivalent to an increased risk for hypercalciuria. For example if the mutation that is detected is the deletion of the entire region, is this deemed an increased risk or the absence of a risk? Thus, claim 1 remains indefinite and applicant's response is considered unpersuasive.

8. Applicant's arguments filed on August 17, 2000 in Paper No. 9 have been considered but were not persuasive. Regarding the rejection under 35 U.S.C. 101 and 112, first paragraph, applicant's arguments were not sufficient to overcome the rejection. At pages 6-7 of the specification refers to the region bounded by D1S2681 to D1S2815 as 4.3 megabases and that it has a "large number of genes encoding a large number of proteins...". The response filed August 17, 2000 refers (item C) to page 6 in regard to credible utility and to MPEP 706.3 (a)(1)+. The comments are unpersuasive since , for example, pages 6-7 do not indicate, for example, how much nor how identification of the or multiple mutation(s) in 4.3 megabases and in one or more of a large number of genes encoding a large number of proteins translates to increased risk. How much of an increased risk is there? Neither this page 6 of the specification nor applicant's response disclose same especially where the claims are directed not to diagnosis/prognosis of AH, but, to ascertaining "increased risk". Additionally, where there is a large number of proteins stated to be encoded by the 4.3 megabases, it is not apparent which one(s) would or would not have been effective to result in "increased risk". Applicant's response also refers to establishing "statistically significant linkage..." but the response does not point out any particular pages or

examples in the application specification directed to the entire region. Note that example 5 in the application only does specific mutations within specific markers. The specification does not, in this example, present correlation of AH to "increased risk". What is the level of increased risk demonstrated in this example? Even where item c of applicant's response asserts no undue experimentation, no indicia are presented for assessing "increased risk". Thus, the comments in applicant's response are unpersuasive.

With regards to applicant's assertions regarding the rejection under 35 U.S.C. 112, first paragraph, the same reasoning applied to the comments made by applicant concerning the rejection under 35 U.S.C. 101 is applicable. A person of ordinary skill in the art would not be to make and use the claimed invention commensurate in scope with the claims because the claimed invention has not demonstrated "increased risk" nor the level of "increased risk". Furthermore, the asserted demonstration of a "statistically significant linkage between a specific genetic loci and the AH phenotype" needs to be pointed to in the specification.

At page 6+ of the response applicant asserts that "it appears that the Action is attempting to couch an enablement rejection in terms of a 101 utility rejection". The claimed invention is enabled for the nucleic acid sequence contained in SEQ ID No. 1 that encodes a protein contained in SEQ ID No. 2, however, does not reasonably provide enablement for any hypercalciuria gene nor a screening method for "increased risk" of AH. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. Eight factors to be considered when determining whether there is sufficient evidence to support a

determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to:

I. Quantity of Experimentation Necessary:

The claimed invention refers to the detection of the presence or absence of a genetic mutation in the genomic region associated with an increased risk of hypercalciuria, it does not teach what gene is associated with hypercalciuria. Therefore, it would warrant undue experimentation for other genes in hypercalciuria (see page 7 of specification). In addition, the specification provides no indicia of the level of increased risk.

II. Amount of direction or guidance presented:

The specification does not disclose one reasonable method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim. Therefore, one skilled in the art at the time of the invention would not be able to make or use the claimed invention.

III. Presence or absence of working examples:

The working examples of the invention are not sufficient to determine the nature and properties of this claimed invention (see Example 5 which only provides a specific mutation within specific markers and this one record is not commensurate in scope with the claims).

IV. Nature of the Invention:

The present invention relates to the discovery that there exists an area on human chromosome 1 that is genetically linked to absorptive hypercalciuria and some forms of osteoporosis. The invention further relates to the development of a familial screening method. The invention is very complex and requires a high level of skill. Additionally, the specification does not disclose many methods for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim.

V. State of the prior art and Relative skill of those in the art:

It is disclosed in the specification that the mechanism by which hypercalciuria leads to osteoporosis is not fully understood (see page 2 of specification). Furthermore, the invention is complex and since there is no analogous art, at the time of the invention a high level of skill is required. Therefore, the specification at the time the application was filed, would not have taught one skilled in the art how to make and or use the full scope of the claimed invention without undue experimentation.

VI. Predictability or unpredictability of the art:

Since very little is known in the prior art about the nature of the invention renders the art unpredictable. The specification should then give more details as to how to make and use the

invention in order to be enabling. One skilled in the art would have a difficult time understanding, using and making the invention as claimed.

VII. Breadth of the claims:

The breadth of the claims are very broad in scope and encompass information not supported in the specification.

For all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

Note that the issues raised in the above rejection are of record in the present application and no new rejections have been applied. For clarity and based on applicant's response regarding the 112, second paragraph rejection the above rejection has been re-instituted from the prior Office action mailed October 21, 1999.

Conclusion

9. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope Robinson whose telephone number is (703) 308-6231. The examiner can normally be reached on Monday-Friday from 9:00 am to 6:00 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low, can be reached at (703) 308-2923.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-4242. Please affix the examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope Robinson, MS

Patent Examiner

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600